(FILE 'HOME' ENTERED AT 15:03:17 ON 04 MAR 2003)

FILE 'CAPLUS, MEDLINE' ENTERED AT 15:03:53 ON 04 MAR 2003

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L1          205 S RNASE? (10N) MOTIF?
L2          154 DUP REM L1 (51 DUPLICATES REMOVED)
L3            3 S L2 AND REVIEW
L4        20739 S RNASE (5N) (A OR T1 OR H OR S OR B OR C OR T2)
L5           75 S L2 (5N) (A OR T1 OR H OR S OR B OR C OR T2)
L6            9 S L5 (10N) (STRUCTURE OR FUNCTION)
L7            0 S L4 (10N) (STRUCTURE ADJ5 FUNCTION)
L8         1762 S L4 (10N) (STRUCTURE OR FUNCTION)
L9            6 S L8 (10N) MOTIF
L10           4 S L9 NOT L6
L11         673 S L4 (10N) DOMAIN?
L12          91 S L11 (10N) (FUNCTION?)
L13          66 DUP REM L12 (25 DUPLICATES REMOVED)
L14           5 S L13 AND REVIEW
L15           9 S L13 AND MOTIF?
L16           9 S L15 NOT RNAASE H
L17          14 S L16 NOT L6 OR L9
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ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1998:162217 CAPLUS
DN 128:280000
TI RNase P and its substrate
AU Kirsebom, Leif A.
CS Department of Microbiology, Biomedical Center, Uppsala, S-751 23, Swed.
SO Many Faces of RNA, [SmithKline Beecham Pharmaceuticals Research Symposia], 8th, Cambridge, UK, Mar., 1997 (1998), 127-144. Editor(s): Eggleston, Drake S.; Prescott, Catherine D.; Pearson, Neil D. Publisher: Academic Press, San Diego, Calif.
CODEN: 65SLAU
DT Conference; General Review
LA English
AB A **review**, with .apprx.45 refs. The ubiquitous RNase P is an endoribonuclease responsible for generating tRNA mols. with matured 5' termini. Bacterial RNase P consists of an RNA subunit and a protein subunit. The RNA alone cleaves various substrates correctly in vitro. The reaction requires the presence of divalent metal ions where Mg2+ promotes cleavage most efficiently. The well-conserved GGU **motif** in Escherichia coli **RNase** P RNA (M1 RNA) base pairs with the 3'-terminal RCAA sequence of a rRNA precursor (interacting residues underlined). This motif is part of an internal loop, P15. Our recent data suggest that the M1 RNA-RCAA interaction plays a role in aligning the scissile bond in the active site such that efficient cleavage is accomplished. M1 RNA is cleaved spontaneously in specific positions as a result of the addn. of divalent ions and two of these cleavage sites are located within P15. The three-dimensional structure of a 31-mer RNA mol. harboring the M1 RNA P15-loop was recently solved by NMR-spectroscopy. Cleavage of various derivs. of the 31-mer RNA, carrying modifications at specific positions within P15, with Mg2+ as well as with Pb2+ showed that this small RNA was cleaved at the same positions as native M1 RNA. These findings suggest that the structure of P15 in the 31-mer RNA is a good approxn. of the structure of this region in M1 RNA. This is further supported by chem. and enzymic structural probing data. Addnl., specific chem. groups in P15 involved in coordinating Mg2+ (or Pb2+) have been identified by using this 31-mer RNA. These data are discussed in view of the three-dimensional structure of the 31-mer RNA as well as in view of the model of cleavage by RNase P RNA.
ST **review** RNase P conformation substrate

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1997:455171 CAPLUS
DN 127:91992
TI A decade of protein engineering on ribonuclease T1. Atomic dissection of the enzyme-substrate interactions
AU Steyaert, Jan
CS Vlaams Interuniversitair instituut Biotechnologie, Dienst Ultrastruktuur, Vrije Universiteit Brussel, Sint-Genesius-Rode, B-1640, Belg.
SO European Journal of Biochemistry (1997), 247(1), 1-11
CODEN: EJBCAI; ISSN: 0014-2956
PB Springer
DT Journal; General Review
LA English
AB A **review** with 91 refs. During the last decade, protein engineering has been used to identify the residues that contribute to the RNase T1-catalyzed transesterification. His-40, Glu-58, and His-92 accelerate the associative nucleophilic displacement at the phosphate atom by the entering 2'-O downstream guanosines in a highly cooperative manner. Glu-58, assisted by the protonated His-40 imidazole, abstrs. a proton from the 2'-O atom, while His-92 protonates the leaving group. Tyr-38, Arg-77, and Phe-100 further stabilize the transition state of the reaction. A functionally independent subsite, including Asn-36 and Asn-98, contributes to chem. turnover by aligning the substrate relative to the catalytic side-chains upon binding of the leaving group. An invariant structural **motif**, involving residues 42-46, renders **RNase** T1 guanine-specific through a series of intermolar H-bonds. Tyr-42 contributes significantly to guanine binding through a parallel face-to-face stacking interaction. Tyr-45, often referred to as the lid of the guanine-binding site, does not contribute to the binding of the

base.

ST **review** RNase T1 mechanism protein engineering

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2000:172671 CAPLUS
DN 133:40336
TI Trypanosoma brucei RNase HI requires its divergent spacer subdomain for enzymatic function and its conserved RNA binding motif for nuclear localization
AU Kobil, J. H.; Campbell, A. G.
CS Box GB-6, Division of Biology and Medicine, Department of Molecular Microbiology and Immunology, Brown University, Providence, RI, USA
SO Molecular and Biochemical Parasitology (2000), 107(1), 135-142
CODEN: MBIPDP; ISSN: 0166-6851
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 9050-76-4, RNase **H**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(I; Trypanosoma brucei **RNase** HI requires its divergent spacer subdomain for enzymic **function** and its conserved RNA binding **motif** for nuclear localization)

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1999:684502 CAPLUS
DN 131:348507
TI Verification of phylogenetic predictions in vivo and the importance of the tetraloop motif in a catalytic RNA
AU Krummel, Daniel A. Pomeranz; Altman, Sidney
CS Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, CT, 06511, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(20), 11200-11205
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB M1 RNA, the catalytic subunit of Escherichia coli **RNase** P, forms **a** secondary **structure** that includes five sequence variants of the tetraloop **motif**. Site-directed mutagenesis of the five tetraloops of M1 RNA, and subsequent steady-state kinetic anal. in vitro, with different substrates in the presence and absence of the protein cofactor, reveal that (i) certain mutants exhibit defects that vary in a substrate-dependent manner, and that (ii) the protein cofactor can correct the mutant phenotypes in vitro, a phenomenon that is also substrate dependent. Thermal denaturation curves of tetraloop mutants that exhibit kinetic defects differ from those of wild-type M1 RNA. Although the data collected in vitro underscore the importance of the tetraloop motif to M1 RNA function and structure, three of the five tetraloops we examd. in vivo are essential for the function of E. coli RNase P. The kinetic data in vitro are not in total agreement with previous phylogenetic predictions but the data in vivo are, as only mutants in those tetraloops proposed to be involved in tertiary interactions fail to complement in vivo. Therefore, the tetraloop motif is crit. for the stabilization of the structure of M1 RNA and essential to RNase P function in the cell.

L10 ANSWER 3 OF 4 MEDLINE
AN 2001362489 MEDLINE
DN 21316523 PubMed ID: 11319219
TI Investigating the structure of human RNase H1 by site-directed mutagenesis.
AU Wu H; Lima W F; Crooke S T
CS Department of Molecular and Structural Biology, Isis Pharmaceuticals, Carlsbad, California 92008, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jun 29) 276 (26) 23547-53.

Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010820
Last Updated on STN: 20030105
Entered Medline: 20010816
AB In this study we examine for the first time the roles of the various domains of human RNase H1 by site-directed mutagenesis. The carboxyl terminus of human RNase H1 is highly conserved with Escherichia coli RNase H1 and contains the amino acid residues of the putative catalytic site and basic substrate-binding domain of the E. coli RNase enzyme. The amino terminus of human **RNase** H1 contains **a** **structure** consistent with a double-strand RNA (dsRNA) binding **motif** that is separated from the conserved E. coli RNase H1 region by a 62-amino acid sequence. These studies showed that although the conserved amino acid residues of the putative catalytic site and basic substrate-binding domain are required for RNase H activity, deletion of either the catalytic site or the basic substrate-binding domain did not ablate binding to the heteroduplex substrate. Deletion of the region between the dsRNA-binding domain and the conserved E. coli RNase H1 domain resulted in a significant loss in the RNase H activity. Furthermore, the binding affinity of this deletion mutant for the heteroduplex substrate was approximately 2-fold tighter than the wild-type enzyme suggesting that this central 62-amino acid region does not contribute to the binding affinity of the enzyme for the substrate. The dsRNA-binding domain was not required for RNase H activity, as the dsRNA-deletion mutants exhibited catalytic rates approximately 2-fold faster than the rate observed for wild-type enzyme. Comparison of the dissociation constant of human RNase H1 and the dsRNA-deletion mutant for the heteroduplex substrate indicates that the deletion of this region resulted in a 5-fold loss in binding affinity. Finally, comparison of the cleavage patterns exhibited by the mutant proteins with the cleavage pattern for the wild-type enzyme indicates that the dsRNA-binding domain is responsible for the observed strong positional preference for cleavage exhibited by human RNase H1.

L10 ANSWER 4 OF 4 MEDLINE
AN 1999432210 MEDLINE
DN 99432210 PubMed ID: 10500154
TI Verification of phylogenetic predictions in vivo and the importance of the tetraloop motif in a catalytic RNA.
AU Pomeranz Krummel D A; Altman S
CS Department of Molecular, Yale University, 266 Whitney Avenue, New Haven, CT 06511, USA.
NC GM-19422 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Sep 28) 96 (20) 11200-5.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991021
AB M1 RNA, the catalytic subunit of Escherichia coli **RNase** P, forms **a** secondary **structure** that includes five sequence variants of the tetraloop **motif**. Site-directed mutagenesis of the five tetraloops of M1 RNA, and subsequent steady-state kinetic analysis in vitro, with different substrates in the presence and absence of the protein cofactor, reveal that (i) certain mutants exhibit defects that vary in a substrate-dependent manner, and that (ii) the protein cofactor can correct the mutant phenotypes in vitro, a phenomenon that is also substrate dependent. Thermal denaturation curves of tetraloop mutants that exhibit kinetic defects differ from those of wild-type M1 RNA. Although the data collected in vitro underscore the importance of the

tetraloop motif to M1 RNA function and structure, three of the five tetraloops we examined in vivo are essential for the function of E. coli RNase P. The kinetic data in vitro are not in total agreement with previous phylogenetic predictions but the data in vivo are, as only mutants in those tetraloops proposed to be involved in tertiary interactions fail to complement in vivo. Therefore, the tetraloop motif is critical for the stabilization of the structure of M1 RNA and essential to RNase P function in the cell.

=>

L14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2002:29538 CAPLUS
DN 136:179613
TI Thirty-three years later, a glimpse at the ribonuclease III active site
AU Zamore, Phillip D.
CS Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, MA, 01655, USA
SO Molecular Cell (2001), 8(6), 1158-1160
CODEN: MOCEFL; ISSN: 1097-2765
PB Cell Press
DT Journal; General Review
LA English
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A **review**. RNase III endonucleases cleave double-stranded RNA, transforming precursor RNAs into mature RNAs that act in pre-mRNA splicing, RNA modification, translation, gene silencing, and the regulation of developmental timing. The recently solved structure of an **RNase** III endonuclease **domain** provides **a** hint at how this family of RNases **functions**.
ST **review** RNase III dsRNA

L14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1998:749265 CAPLUS
DN 130:135651
TI Ribonucleases H of Saccharomyces cerevisiae, Schizosaccharomyces pombe, Crithidia fasciculata and Neurospora crassa
AU Crouch, R. J.; Cerritelli, S. M.
CS Section on Formation of RNA, Laboratory of Molecular Genetics, National, U.S. National Institutes of Health, Bethesda, MD, 20892-2790, USA
SO Ribonucleases H (1998), 79-100. Editor(s): Crouch, Robert J.; Toulme, Jean-Jacques. Publisher: INSERM, Paris, Fr.
CODEN: 66ZRAM
DT Conference; General Review
LA English
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A **review** with 60 refs. on RNases H of lower eukaryotes. The questions addressed are: the no. of RNases H in an individual organism; the cellular localization of the enzymes; their relationship to the cell cycle; properties of strains with deletions of the RNase H region; the division of these RNases **H** into an **RNase H** **domain** and **a** non-**RNase H** **domain** and the **function**(**s**) of the non-**RNase H domain**; the relationships of these enzymes to RNases H of from higher eukaryotes.
ST **review** RNase H lower eukaryote

L14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1992:545756 CAPLUS
DN 117:145756
TI RNase H: three-dimensional structure and function
AU Morikawa, K.; Katayanagi, K.
CS Protein Eng. Res. Inst., Suita, 565, Japan
SO Bulletin de l'Institut Pasteur (Paris) (1992), 90(2), 71-82
CODEN: BIPAA8; ISSN: 0020-2452
DT Journal; General Review
LA English
AB A **review** with 42 refs. on recent progress in the 3-dimensional structural anal. of Escherichia coli RNase H and the HIV-1 virus RNase H domain of reverse transcriptase. The relations between the tertiary structure and functions of RNase H are discussed, with particular focus on the RNase H activity of retroviral reverse transcriptase.
ST **review** RNase H structure function
IT 9068-38-6, Reverse transcriptase
RL: PRP (Properties)
(**RNase H domain** of, of HIV-1 virus, structure-**function** relations of)

L14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1992:526876 CAPLUS
DN 117:126876
TI The destiny of reverse transcriptase anatomy
AU Hughes, Stephen H.
CS Frederick Cancer Res. Dev. Cent., NCI, Frederick, 21702-1201, USA
SO Current Biology (1991), 1(5), 323-5
CODEN: CUBLE2; ISSN: 0960-9822
DT Journal; General Review
LA English
AB A **review** with 18 refs. The structure of the RNase H domain of HIV-1 reverse transcriptase has been solved. Comparison with that of Escherichia coli RNase H provides clues to the **functional** inactivity of the sep. HIV-1 **RNase H domain**.
ST **review** reverse transcriptase HIV1 virus; RNase H HIV1 reverse transcriptase **review**

L14 ANSWER 5 OF 5 MEDLINE
AN 1999203068 MEDLINE
DN 99203068 PubMed ID: 10189185
TI Cytotoxic T-lymphocyte responses to HIV-1 reverse transcriptase (**review**).
AU Menendez-Arias L; Mas A; Domingo E
CS Centro de Biologia Molecular "Severo Ochoa", CSIC-Universidad Autonoma de Madrid, Cantoblanco, Spain.
SO VIRAL IMMUNOLOGY, (1998) 11 (4) 167-81. Ref: 81
Journal code: 8801552. ISSN: 0882-8245.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; AIDS
EM 199905
ED Entered STN: 19990614
Last Updated on STN: 19990614
Entered Medline: 19990528
TI Cytotoxic T-lymphocyte responses to HIV-1 reverse transcriptase (**review**).
AB Cytotoxic T lymphocytes (CTL) play an important role in the control of human immunodeficiency virus (HIV) infection. CTL responses have been demonstrated for most of the HIV gene products, predominantly gag, pol, and env-encoded proteins, and also for the regulatory proteins Nef, Tat, Vif, or Rev. The HIV-1 reverse transcriptase (RT), which derives from expression of the pol gene, is an important target of cellular immune responses in infected individuals. More than 40 different peptides containing RT-specific CTL epitopes have been identified. The most conserved and frequently detected are located in the 'fingers' and 'palm' subdomains of the enzyme, but other epitopes have been found in the 'thumb' and 'connection' subdomains as well as in the **RNase H domain**. Studies on the sequence variability and **functional** role of amino acids forming CTL epitopes are relevant for addressing important questions relative to viral escape from immmune control and the future design of anti-AIDS vaccines.

=>

L15 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2002:45228 CAPLUS
DN 136:163186
TI Reversible substrate-induced domain motions in ribonuclease A
AU Vitagliano, Luigi; Merlino, Antonello; Zagari, Adriana; Mazzarella, Lelio
CS Centro di Biocristallografia, CNR, Naples, Italy
SO Proteins: Structure, Function, and Genetics (2001), Volume Date 2002, 46(1), 97-104
CODEN: PSFGEY; ISSN: 0887-3585
PB Wiley-Liss, Inc.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Protein **motifs**
(crystal structure of RNase A reveals binding of substrate analogs to RNase A induces subtle domain motion that may play role in binding and release of substrate)
IT Enzyme **functional** sites
(substrate-binding; crystal structure of **RNase A** reveals binding of substrate analogs to RNase A induces subtle **domain** motion that may play role in binding and release of substrate)

L15 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2001:829520 CAPLUS
DN 136:321203
TI Insertion of a peptide from MuLV RT into the connection subdomain of HIV-1 RT results in a functionally active chimeric enzyme in monomeric conformation
AU Pandey, Pradeep K.; Kaushik, Neerja; Talele, Tanaji T.; Yadav, Prem N. S.; Pandey, Virendra N.
CS Center for the Study of Emerging and Re-Emerging Pathogens, Department of Biochemistry and Molecular Biology, UMD-New Jersey Medical School, Newark, NJ, 07103, USA
SO Molecular and Cellular Biochemistry (2001), 225(1&2), 135-144
CODEN: MCBIB8; ISSN: 0300-8177
PB Kluwer Academic Publishers
DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The natural form of the human immunodeficiency virus type one reverse transcriptase (HIV-1 RT) found in virion particles is a heterodimer composed of the p66 and p51 subunits. The catalytic activity resides in the larger subunit in the heterodimeric (p66/p51) enzyme while in the monomeric form it is inactive. In contrast, Murine leukemia virus RT (MuLV RT) is functionally active in the monomeric form. In the primary amino acid sequence alignment of MuLV RT and HIV-1 RT, we have identified three specific regions in MuLV RT, that were missing in HIV-1 RT. In a sep. study, we have shown that a chimeric RT construct comprising of the polymerase **domain** of HIV-1 RT and **RNase-H** **domain** of MuLV RT is **functionally** active as monomer. In this communication, we demonstrate that insertion of a peptide (corresponding to amino acid residues 480-506) from the connection subdomain of MuLV RT into the connection subdomain of HIV-1 RT (between residues 429 and 430) results in a functionally active monomeric chimeric RT. Furthermore, this chimeric enzyme does not dimerize with exogenously added p51 subunit of HIV-1 RT. Functional anal. of the chimeric RT revealed template specific variations in its catalytic activity. The chimeric enzyme catalyzes DNA synthesis on both heteropolymeric DNA and homopolymeric RNA (poly rA) template but curiously lacks reverse transcriptase ability on heteropolymeric RNA template. Similar to MuLV RT, the polymerase activity of the chimeric enzyme is not affected by acetonitrile, a reagent which dissocs. dimeric HIV-1 RT into inactive monomers. These results together with a proposed 3-D mol. model of the chimeric enzyme suggests that the insertion of the missing region may induce a change in the spatial position of **RNase H** **domain** such that it is **functionally** active in monomeric

conformation.
IT Protein **motifs**
(connection subdomain; insertion of a peptide from MuLV RT into the connection subdomain of HIV-1 RT results in a functionally active chimeric enzyme in monomeric conformation)

L15 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2001:166204 CAPLUS
DN 134:322661
TI A domain-swapped RNase A dimer with implications for amyloid formation
AU Liu, Yanshun; Gotte, Giovanni; Libonati, Massimo; Eisenberg, David
CS UCLA-DOE Laboratory of Structural Biology and Molecular Medicine, Department of Chemistry and Biochemistry and Biological Chemistry, University of California, Los Angeles, CA, 90095-1570, USA
SO Nature Structural Biology (2001), 8(3), 211-214
CODEN: NSBIEW; ISSN: 1072-8368
PB Nature America Inc.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Crystal structure
Enzyme **functional** sites
Protein **motifs**
(**domain**-swapped **RNase A** dimer with implications for amyloid formation)

L15 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2000:318803 CAPLUS
DN 133:173837
TI Interaction of p55 reverse transcriptase from the Saccharomyces cerevisiae retrotransposon Ty3 with conformationally distinct nucleic acid duplexes
AU Rausch, Jason W.; Grice, Marion K. Bona-Le; Nymark-McMahon, M. Henrietta; Miller, Jennifer T.; Le Grice, Stuart F. J.
CS Human Immunodeficiency Virus Drug Resistance Program, Division of Basic Sciences, NCI-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA
SO Journal of Biological Chemistry (2000), 275(18), 13879-13887
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The 55-kDa reverse transcriptase (RT) domain of the Ty3 POL3 open reading frame was purified and evaluated on conformationally distinct nucleic acid duplexes. Purified enzyme migrated as a monomer by size exclusion chromatog. Enzymic footprinting indicate Ty3 RT protects template nucleotides +7 through -21 and primer nucleotides -1 through -24. Contrary to previous data with retroviral enzymes, a 4-base pair region of the template-primer duplex remained nuclease accessible. The C-terminal portion of Ty3 RT encodes **a functional RNase H domain**, although the hydrolysis profile suggests an increased spatial sepn. between the catalytic centers. Despite conservation of catalytically important residues in the RNase H domain, Fe2+, fails to replace Mg2+ in the RNase H catalytic center for localized generation of hydroxyl radicals, again suggesting this domain may be structurally distinct from its retroviral counterparts. RNase H specificity was investigated using a model system challenging the enzyme to select the polypurine tract primer from within an RNA/DNA hybrid, extend this into (+) DNA, and excise the primer from nascent DNA. Purified RT catalyzed each of these three steps but was almost inactive on a non-polypurine tract RNA primer. Our studies provide the first detailed characterization of the enzymic activities of a retrotransposon reverse transcriptase.
IT Protein **motifs**
(DNA polymerase and RNase H domains of Saccharomyces cerevisiae retrotransposon reverse transcriptase)

L15 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 1997:755466 CAPLUS
DN 128:151051
TI A putative nucleic acid-binding domain in Bloom's and Werner's syndrome helicases
AU Morozov, Vladimir; Mushegian, Arcady R.; Koonin, Eugene V.; Bork, Peer
CS Bioscience AG, LION, Heidelberg, Germany
SO Trends in Biochemical Sciences (1997), 22(11), 417-418
CODEN: TBSCDB; ISSN: 0376-5067
PB Elsevier Science Ltd.
DT Journal
LA English
AB Aside from a helicase domain no other **motifs** indicative of function are known in Werner's and Bloom's syndrome proteins (WRNp and BLMp). Here, a C-terminal domain, referred to as HRDC (Helicase and RNase D C-terminal), has been identified in WRNp, BLMp and related helicases. The domain appears to be non-essential since it is absent in RecQ-like helicases from several species. The presence of this domain only in proteins from purple bacteria and eukaryotes (M. leprae UvrD being an exception) suggest a mitochondrial genome origin. The HRDC domain may play a role in nucleic acid-binding. A considerable no. of mutations in WRNp have been mapped to the HRDC domain. No mutations have yet been mapped to BLMp HRDC domain. The role of the HRDC domain mutations in the pathogenesis of Werner's and Bloom's syndrome and more generally in genome stability remains to be established.
IT Enzyme **functional** sites
Protein **motifs**
(HRDC (Helicase and **RNase** D **C**-terminal); identification of putative nucleic acid-binding **domain** in human Bloom's and Werner's syndrome helicases)

L15 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 1997:364691 CAPLUS
DN 127:62472
TI Exchanging sequence domains between S-RNases from Nicotiana alata disrupts pollen recognition
AU Zurek, Daniel M.; Mou, Beiquan; Beecher, Brian; McClure, Bruce
CS Department of Biochemistry, University of Missouri-Columbia, Columbia, MO, 65211, USA
SO Plant Journal (1997), 11(4), 797-808
CODEN: PLJUED; ISSN: 0960-7412
PB Blackwell
DT Journal
LA English
AB In self-incompatible plants of the Solanaceae, the specificity of pollen rejection is controlled by a single multiallelic S-locus. Pollen tube growth is inhibited in the style when its single S-allele matches either S-allele present in the diploid pistil. Each S-allele encodes an S-RNase with a unique sequence. S-RNases are secreted into the extra-cellular matrix of the transmitting tract which guides pollen tubes toward the ovary. Although it is known that S-RNases are the determinants of S-allele specificity in the pistil, it is not known how allele-specific information is encoded in the sequence. Therefore, we exchanged domains between S-RNases with different recognition specificities and expressed the chimeric proteins in transgenic plants to det. their effects on pollination behavior. Nine chimeric constructs were prepd. in which domains from Nicotiana alata SA2- and SC10-RNases were exchanged. Among these nine constructs, the entire S-RNase sequence was sampled by exchanging single variable domains as well as larger blocks of contiguous sequences. The chimeric S-RNases retained enzymic activity and were expressed at levels comparable to control transformants expressing SA2- and SC10-RNase. However, none of the chimeric S-RNases caused rejection of either SA2- or SC10-pollen. We conclude that the recognition function of S-RNases can be disrupted by alterations in many parts of the sequence. It appears that the recognition **function** of **S-RNase** is not localized to **a** specific **domain**.
IT Protein **motifs**
(domain exchange; exchanging sequence domains between S-RNases from Nicotiana alata disrupts pollen recognition)

L15 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 1995:613647 CAPLUS
DN 123:50915
TI The non-RNase H domain of Saccharomyces cerevisiae RNase H1 binds double-stranded RNA: magnesium modulates the switch between double-stranded RNA binding and RNase H activity
AU Cerritelli, Susana M.; Crouch, Robert J.
CS Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, Bethesda, MD, 20892, USA
SO RNA (1995), 1(3), 246-59
CODEN: RNARFU; ISSN: 1355-8382
PB Cambridge University Press
DT Journal
LA English
AB Eukaryotic RNases H of known sequence are composed of an RNase H domain similar in size and sequence to that of Escherichia coli RNase HI and addnl. domains of unknown function. The RNase H1 of Saccharomyces cerevisiae has such an RNase H domain at its C-terminus. Here the authors show that the N-terminal non-RNase H portion of the yeast RNase H1 binds tightly to double-stranded RNA (dsRNA) and RNA-DNA hybrids even in the absence of the RNase H domain. Two copies of a sequence with limited similarity to the dsRNA-binding **motif** are present in this N-terminus. When the first of these sequences is altered, the protein no longer binds tightly to dsRNA and exhibits an increase in RNase H activity. Unlike other dsRNA-binding proteins, increasing the Mg2+ concn. from 0.5 mM to 5 mM inhibits binding of RNase H1 to dsRNA; yet a protein missing the RNase H domain binds strongly to dsRNA even at the higher Mg2+ concn. These results suggest that binding to dsRNA and RNase H activity are mutually exclusive, and the Mg2+ concn. is crit. for switching between the activities. Changes in the Mg2+ concn. or proteolytic severing of the dsRNA-binding domain could alter the activity or location of the RNase H and may govern access of the enzyme to the substrate. Sequences similar to the dsRNA-binding **motif** are present in other eukaryotic RNases H and the transactivating protein of cauliflower mosaic virus, suggesting that these proteins may also bind to dsRNA.
IT Enzyme **functional** sites
Saccharomyces cerevisiae
(non-**RNase H domain** of Saccharomyces cerevisiae **RNase** H1 binds double-stranded RNA)

L15 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 1995:208332 CAPLUS
DN 122:49962
TI Characterization of a unique protein component of yeast RNase MRP: an RNA-binding protein with a zinc-cluster domain
AU Schmitt, Mark E.; Clayton, David A.
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SO Genes & Development (1994), 8(21), 2617-28
CODEN: GEDEEP; ISSN: 0890-9369
PB Cold Spring Harbor Laboratory Press
DT Journal
LA English
AB RNase MRP is a ribonucleoprotein endoribonuclease that has been shown to cleave mitochondrial primer RNA sequences from a variety of sources. Most of the RNase MRP activity is found in the nucleus where it plays a role in the processing of 5.8 S rRNA. A temp.-conditional point mutation in the yeast RNA component of the enzyme has been identified. This mutation results in a loss of normal rRNA processing at the nonpermissive temp. while cellular levels of the RNA component of RNase MRP remain stable. High-copy suppressor anal. of this point mutation was employed to identify interacting proteins. A unique suppressor, termed SNM1 (suppressor of nuclear mitochondrial endoribonuclease 1), was identified repeatedly. The SNM1 gene was localized to the right arm of chromosome IV, directly adjacent to the SNF1 gene, and it contains an open reading frame encoding a protein of 198 amino acids. The protein contains a leucine zipper **motif**, a zinc-cluster **motif**, and a serine/lysine-rich tail. The gene was essential for viability in a yeast cell, consistent with it being a protein component of the RNase MRP ribonucleoprotein

complex. Recombinant SNM1 protein binds RNA in both gel retardation and Northwestern assays. Antibodies raised against bacterially expressed proteins identified 4 sep. species in yeast whole cell exts. Antibodies directed against the SNM1 protein immunopptd. RNase MRP RNA from whole-cell exts. without pptg. the structurally and functionally related RNase P RNA. The SNM1 protein may be an essential and specific component of the RNase MRP ribonucleoprotein complex, the first unique protein of this complex to be identified.

IT Saccharomyces cerevisiae
(characterization and **function** of **a** protein component of yeast **RNase** MRP with **a** zinc-cluster **domain**)

IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(SNM1, characterization and **function** of **a** protein component of yeast **RNase** MRP with **a** zinc-cluster **domain**)

IT 160124-98-1
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; characterization and **function** of **a** protein component of yeast **RNase** MRP with **a** zinc-cluster **domain**)

IT 123082-54-2, **RNase** MRP
RL: PRP (Properties)
(characterization and **function** of **a** protein component of yeast **RNase** MRP with **a** zinc-cluster **domain**)

IT 159071-96-2
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; characterization and **function** of **a** protein component of yeast **RNase** MRP with **a** zinc-cluster **domain**)

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AN 1993:490026 CAPLUS
DN 119:90026
TI Three-dimensional structural resemblance between the ribonuclease H and connection domains of HIV reverse transcriptase and the ATPase fold revealed using graph theoretical techniques
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SO FEBS Letters (1993), 324(1), 15-21
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB 3D searching techniques based on algorithms derived from graph theory were used to establish two previously unreported structural similarities involving the RNase H domain of HIV-1 reverse transcriptase (RT). First, it is reported that there is a strong similarity between the 3D folds of the RNase H domain of RT and the 'ATPase folds' of hexokinase, the 70 kDa heat-shock cognate protein and actin. Like RNase H, these enzymes are involved in nucleotide binding and metal ion-catalyzed cleavage of a phosphodiester bond. Similarities of the folding **motif** and the position of the metal-binding site in these enzymes suggest possible functional analogies and evolutionary relationships with RNase H. Second, there is a strong resemblance between the folds of the RNase H domain and of the p66 and p51 'connection' domains of RT. It is possible that this striking similarity within the RT structure indicates a possible ancestral gene doubling event. The similarity may also indicate that the connection domains possess functional roles in addn. to those previously suggested, and they may therefore represent a further target for the design of therapeutic agents.

IT Enzyme **functional** sites
(of reverse transcriptase, of HIV-1, **RNase H**

domain, three-dimensional structure of, ATPase fold and connection **domains** similarity to)

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